IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	William P. Van Antwerp et al.	Examiner:	Margaret Moore
Serial No.:	Not Yet Assigned	Group Art Unit:	1712
Filed:	August 21, 2001	Docket:	G&C 130.15-US-D1
Title:	DETECTION OF BIOLOGICAL MOLECULES USING CHEMICAL AMPLIFICATION AND OPTICAL SENSORS		

CERTIFICATE OF MAILING UNDER 37 CFR 1.10
'Express Mail' mailing label number: EL815952591US
Date of Deposit: August 21, 2001
I hereby certify that this paper or fee is being deposited with the United States Postal Service 'Express Mail Post Office To Addressee' service under 37 CFR 1.10 and is addressed to the Commissioner for Patents, Washington, D.C. 20231.
By: Isabell Ogata
Name: Isabell Ogata

PRELIMINARY AMENDMENT

Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

Prior to a first Office Action, please amend the above-identified application as follows:

IN THE SPECIFICATION

Please replace the paragraph on page 1, lines 5-12 with the following paragraph:

This application is a Divisional application of U. S. Patent Application Serial No. 09/401,147, filed September 22, 1999 which is a Continuation Application of and claims the benefit of U.S. Patent Application Serial No. 08/752,945, filed November 21, 1996, now U.S. Patent No. 6,011,984, which is a Continuation–in-Part of U.S. Provisional Application Serial No. 60/007,515, (filed November 22, 1995) and is related to U.S. Patent Application Serial No. 08/721,262, filed September 26, 1996, now U.S. Patent No. 5,777,060 which is a Continuation-in-Part of U.S. Patent Application Serial No. 08/410,775, filed March 27, 1995, now abandoned, the disclosures of each being incorporated herein by reference. The United States Government may have rights in inventions disclosed in this application pursuant to Contract No. W-7405-ENG-48 between the United States Department of Energy and the University of California for the operation of Lawrence Livermore National Laboratory.

Please replace the paragraph on page 16, lines 13-18 with the following paragraph:

The substrate layer can be prepared from a polymer such as a polyurethane, silicone, silicon-containing polymer, chronoflex, P-HEMA or sol-gel. The substrate layer can be permeable to the analyte of interest, or it can be impermeable. For those embodiments in which the substrate layer is impermeable, the amplification components will be coated on the exterior of the substrate layer and further coated with a permeable layer (see FIG. 14A).

Please replace the paragraph spanning pages 16 and 17 with the following paragraph:

For those embodiments in which a polymer matrix is to be placed in contact with a tissue or fluid, the polymer matrix will preferably be a biocompatible matrix. In addition to being biocompatible, another requirement for this outermost layer of an implantable amplification system is that it be permeable to the analyte of interest. A number of biocompatible polymers are known, including some recently described silicon-containing polymers (see Copending application Ser. No. 08/721,262, filed Sep. 26, 1996, now U.S. Patent No. 5,777,060, and incorporated herein by reference) and hydrogels (see Copending application Ser. No. 08/749,754, filed Oct. 24, 1996, now U.S. Patent No. 5,786,439 , and incorporated herein by reference). Silicone-containing polyurethane can be used for the immobilization of most of the glucose binding systems or other analyte amplification components. Other polymers such as silicone rubbers (NuSil 4550), biostable polyurethanes (Biomer, Tecothane, Tecoflex, Pellethane and others), PEEK (polyether ether ketone) acrylics or combinations are also suitable.

Please replace the paragraph on page 17, lines 9-20 with the following paragraph:

In one group of embodiments, the amplification components are either entrapped in, or covalently attached to a silicone-containing polymer. This polymer is a homogeneous matrix prepared from biologically acceptable polymers whose hydrophobic/hydrophilic balance can be varied over a wide range to control the rate of polyhydroxylated analyte diffusion to the amplification components. The matrix can be prepared by conventional methods by the polymerization of diisocyanates, hydrophilic diols or diamines, silicone polymers and optionally, chain extenders. The resulting polymers are soluble in solvents such as acetone or ethanol and may be formed as a matrix from solution by dip, spray or spin coating. Preparation of biocompatible matrices for glucose monitoring have been described in co-pending applications Ser. Nos.

08/721,262, now U.S. Patent No. 5,777,060, and 08/749,754, now U.S. Patent No. 5,786,439, the disclosures of which have previously been incorporated herein by reference.

Please replace the paragraph on page 20, lines 20-28 with the following paragraph:

In some embodiments, the polymer matrix containing the amplification components can be further coated with a permeable layer such as a hydrogel, cellulose acetate, P-HEMA, nafion, or glutaraldehyde. A number of hydrogels are useful in the present invention. For those embodiments in which glucose monitoring is to be conducted, the preferred hydrogels are those which have been described in co-pending application Ser. No. 08/749,754, now U.S. Patent No. 5,786,439, the disclosure of which has previously been incorporated herein by reference. Alternatively, hydrogels can be used as the polymer matrix which encase or entrap the amplification components. In still other embodiments, the amplification components can be covalently attached to a hydrogel.

Please replace the paragraph on page 31, lines 25-26 with the following paragraph:

Other suitable silicone-containing polymers are described in co-pending application Ser. No. 08/721,262, now U.S. Patent No. 5,777,060.

IN THE CLAIMS

Please cancel claims 1-20 and add claims 21-50 as follows:

--21. (NEW) A biocompatible polymer matrix comprising an amplification component capable of producing a polyhydroxylated analyte signal upon interrogation by an optical system, wherein said amplification component requires a photo-induced electron transfer for production of said signal.--

--22. (NEW) The biocompatible polymer matrix in accordance with claim 21, wherein said biocompatible polymer matrix is a solid substrate.--

--23. (NEW) The biocompatible polymer matrix in accordance with claim 22, wherein said solid substrate is a member selected from the group consisting of polyurethane, silicon, silicon-containing polymer, chronoflex, P-HEMA or sol-gel.--

--24. (NEW) The biocompatible polymer matrix in accordance with claim 21, wherein said biocompatible polymer matrix comprises a hydrophilic polymer.--

--25. (NEW) The biocompatible polymer matrix in accordance with claim 21, wherein said biocompatible polymer is a member selected from the group consisting of a polyurethane, a silicone, an acrylic, and a silicone containing polyurethane.--

--26. (NEW) The biocompatible polymer matrix in accordance with claim 21, wherein said biocompatible polymer matrix is a member selected from the group consisting of a disk, a cylinder, a patch, a microsphere and a refillable sack.--

--27. (NEW) The biocompatible polymer matrix in accordance with claim 26, wherein said biocompatible polymer matrix is a microsphere.--

--28. (NEW) The biocompatible polymer matrix in accordance with claim 21, wherein said biocompatible polymer matrix is implanted subdermally.--

--29. (NEW) The biocompatible polymer matrix in accordance with claim 21, wherein said biocompatible polymer matrix is permeable to glucose.--

--30. (NEW) The biocompatible polymer matrix in accordance with claim 21, wherein said biocompatible polymer matrix is permeable to oxygen.--

--31. (NEW) The biocompatible polymer matrix in accordance with claim 21, wherein said biocompatible polymer matrix is optically transparent.--

--32. (NEW) The biocompatible polymer matrix in accordance with claim 21, further comprising a biocompatible shell.--

--33. (NEW) The biocompatible polymer matrix in accordance with claim 32, wherein said biocompatible shell is a member selected from the group consisting of dialysis fiber, teflon cloth, resorbable polymers and islet encapsulation materials.--

--34. (NEW) The biocompatible polymer matrix in accordance with claim 21, further comprising a mesh.--

--35. (NEW) The biocompatible polymer matrix in accordance with claim 21, wherein said amplification component is covalently attached to said biocompatible polymer matrix.--

--36. (NEW) The biocompatible polymer matrix in accordance with claim 21, wherein said amplification component comprises a boronic acid moiety.--

--37. (NEW) A biocompatible polymer matrix comprising a fluorescent transducer component that binds polyhydroxylate analyte and whose fluorescence is modulated by a photo-induced electron transfer process, wherein upon illumination of the fluorescent transducer component in the presence of polyhydroxylate analyte a change in fluorescence is observable that is correlatable with the concentration of bound polyhydroxylate analyte.--

--38. (NEW) The biocompatible polymer matrix of claim 37, wherein the change in fluorescence is measured as a change in fluorescent intensity.--

--39. (NEW) The biocompatible polymer matrix of claim 37, wherein the change in fluorescence is measured as a change in the average fluorescent lifetime of the fluorescent transducer component.--

--40. (NEW) The biocompatible polymer matrix of claim 37, wherein polyhydroxylate analyte binding to the fluorescent transducer component produces an increase in the fluorescence of the fluorescent transducer component.--

--41. (NEW) The biocompatible polymer matrix of claim 37, wherein polyhydroxylate analyte binding to the fluorescent transducer component produces a decrease in the fluorescence of the fluorescent transducer component.--

--42. (NEW) The biocompatible polymer matrix of claim 37, wherein the photo-induced electron transfer process of the fluorescent transducer component is modulated by polyhydroxylate analyte binding.--

--43. (NEW) The biocompatible polymer matrix in accordance with claim 37, wherein said fluorescent transducer component comprises a boronic acid moiety.--

--44. (NEW) A biocompatible polymer matrix comprising an amplification component capable of producing a signal upon interrogation by an optical system, wherein the signal is modulated by polyhydroxylate analyte binding and wherein polyhydroxylate analyte binding modulates a photo-induced electron transfer process.--

--45. (NEW) The biocompatible polymer matrix of claim 44, wherein the signal is measured as a change in fluorescent intensity of the amplification component.--

--46. (NEW) The biocompatible polymer matrix of claim 44, wherein the signal is measured as a change in the average fluorescent lifetime of the amplification component.--

--47. (NEW) The biocompatible polymer matrix of claim 44, wherein bound polyhydroxylate analyte produces an increase in the signal.--

--48. (NEW) The biocompatible polymer matrix of claim 44, wherein bound polyhydroxylate analyte produces a decrease in the signal.--

--49. (NEW) The biocompatible polymer matrix of claim 44, wherein the photo-induced electron transfer process is modulated by bound polyhydroxylate analyte.--

--50. (NEW) The biocompatible polymer matrix in accordance with claim 44, wherein said amplification component comprises a boronic acid moiety.--

REMARKS

Prior to a first Office Action in this application, Applicants request that original claims 1-20 be cancelled and new claims 21-50 be added. The new claims in this divisional application do not involve any new matter or objectionable changes. In particular, claims drawn to a biosensor including a biocompatible matrix, classified in class 600, subclass 317 were subject to a restriction requirement in the parent application, United States Patent Application Serial No. 09/401,147 (a copy of the Office Action requiring this restriction is attached herein as Exhibit A). Accordingly these claims are presented in this divisional application. When the Examiner takes this application up for action, she is requested to take the foregoing into account.

It is submitted that this application is now in good order for allowance and such allowance is respectively solicited. Should the Examiner believe minor matters still remain that can be resolved in a telephone interview, the Examiner is urged to call Applicants' undersigned attorney.

Respectfully submitted,

William P. Van Antwerp et al.

By their attorneys,

GATES & COOPER LLP

6701 Center Drive West, Suite 1050
Los Angeles, California 90045
(310) 641-8797

Date: August 21, 2001

By: _____
Name: William J. Wood
Reg. No.: 42,236

WJW/sjm

APPENDIX : SPECIFICATION IN MARKED-UP FORM

Please replace the paragraph on page 1, lines 5-12 with the following paragraph:

This application is a Divisional application of U. S. Patent Application Serial No. 09/401,147, filed September 22, 1999 which is a Continuation Application of and claims the benefit of U.S. Patent Application Serial No. 08/752,945, filed November 21, 1996, now U.S. Patent No. 6,011,984, which is a Continuation–in-Part of U.S. Provisional Application Serial No. 60/007,515, (filed November 22, 1995) and is related to [USSN] U.S. Patent Application Serial No. 08/721,262[(Attorney Docket 17898-000410)], filed September 26, 1996, now U.S. Patent No. 5,777,060 which is a Continuation-in-Part of [USSN] U.S. Patent Application Serial No. 08/410,775, filed March 27, 1995, now abandoned, the disclosures of each being incorporated herein by reference. The United States Government may have rights in inventions disclosed in this application pursuant to Contract No. W-7405-ENG-48 between the United States Department of Energy and the University of California for the operation of Lawrence Livermore National Laboratory.

Please replace the paragraph on page 16, lines 13-18 with the following paragraph:

The substrate layer can be prepared from a polymer such as a polyurethane, silicone, silicon-containing polymer, chronoflex, P-HEMA or sol-gel. The substrate layer can be permeable to the analyte of interest, or it can be impermeable. For those embodiments in which the substrate layer is impermeable, the amplification components will be coated on the exterior of the substrate layer and further coated with a permeable layer (see FIG. 14A).

Please replace the paragraph spanning pages 16 and 17 with the following paragraph:

For those embodiments in which a polymer matrix is to be placed in contact with a tissue or fluid, the polymer matrix will preferably be a biocompatible matrix. In addition to being biocompatible, another requirement for this outermost layer of an implantable amplification system is that it be permeable to the analyte of interest. A number of biocompatible polymers are known, including some recently described silicon-containing polymers (see Copending application Ser. No. 08/721,262, filed Sep. 26, 1996, now U.S. Patent No. 5,777,060, and incorporated herein by reference) and hydrogels (see Copending application Ser. No. 08/749,754, filed Oct. 24, 1996, now U.S. Patent No. 5,786,439 [Attorney docket Number 017898-000300], and incorporated herein by reference). Silicone-containing polyurethane can be used for the immobilization of most of the glucose binding systems or other analyte amplification components. Other polymers such as

silicone rubbers (NuSil 4550), biostable polyurethanes (Biomer, Tecothane, Tecoflex, Pellethane and others), PEEK (polyether ether ketone) acrylics or combinations are also suitable.

Please replace the paragraph on page 17, lines 9-20 with the following paragraph:

In one group of embodiments, the amplification components are either entrapped in, or covalently attached to a silicone-containing polymer. This polymer is a homogeneous matrix prepared from biologically acceptable polymers whose hydrophobic/hydrophilic balance can be varied over a wide range to control the rate of polyhydroxylated analyte diffusion to the amplification components. The matrix can be prepared by conventional methods by the polymerization of diisocyanates, hydrophilic diols or diamines, silicone polymers and optionally, chain extenders. The resulting polymers are soluble in solvents such as acetone or ethanol and may be formed as a matrix from solution by dip, spray or spin coating. Preparation of biocompatible matrices for glucose monitoring have been described in co-pending applications Ser. Nos. 08/721,262, now U.S. Patent No. 5,777,060, and 08/749,754, now U.S. Patent No. 5,786,439, the disclosures of which have previously been incorporated herein by reference.

Please replace the paragraph on page 20, lines 20-28 with the following paragraph:

In some embodiments, the polymer matrix containing the amplification components can be further coated with a permeable layer such as a hydrogel, cellulose acetate, P-HEMA, nafion, or glutaraldehyde. A number of hydrogels are useful in the present invention. For those embodiments in which glucose monitoring is to be conducted, the preferred hydrogels are those which have been described in co-pending application Ser. No. 08/749,754, now U.S. Patent No. 5,786,439, the disclosure of which has previously been incorporated herein by reference. Alternatively, hydrogels can be used as the polymer matrix which encase or entrap the amplification components. In still other embodiments, the amplification components can be covalently attached to a hydrogel.

Please replace the paragraph on page 31, lines 25-26 with the following paragraph:

Other suitable silicone-containing polymers are described in co-pending application Ser. No. 08/721,262, now U.S. Patent No. 5,777,060.

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 21 - 36, 44 - 54, and 59 - 64, drawn to a biosensor including a biocompatible polymer matrix, classified in class 600, subclass 317.

II. Claims 37 - 43, drawn to a method of preparing a biocompatible polymer matrix, classified in class 424, subclass 484.

III. Claims 55 - 58, drawn to a method of immobilizing a boronic acid moiety in a solid support, classified in class 422, subclass 82.01.

The inventions are distinct, each from the other because of the following reasons:

2. Inventions I and II are related as process of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case the product made by Group II can be used as a coating for an implantable device.

3. Inventions II and III are related as subcombinations disclosed as usable together in a single combination. The subcombinations are distinct from each other if they are shown to be separately usable. In the instant case, invention II has separate utility such as a method for preparing a coating for an implantable device. See MPEP § 806.05(d).

4. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

5. A telephone call was made to Joseph Snyder on September 25, 2000 to request an oral election to the above restriction requirement, but did not result in an election being made.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

6. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eric F Winakur whose telephone number is (703) 308-3940. The examiner can normally be reached on Mon. - Thurs. from 7:30 am - 5:00 pm and on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cary O'Connor can be reached on (703) 308-2701. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-0758 for regular communications and (703) 308-0758 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0858.

Eric F Winakur
Primary Examiner
Art Unit 3736

October 2, 2000